U.S. DEPARTMENT OF
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NATIONAL
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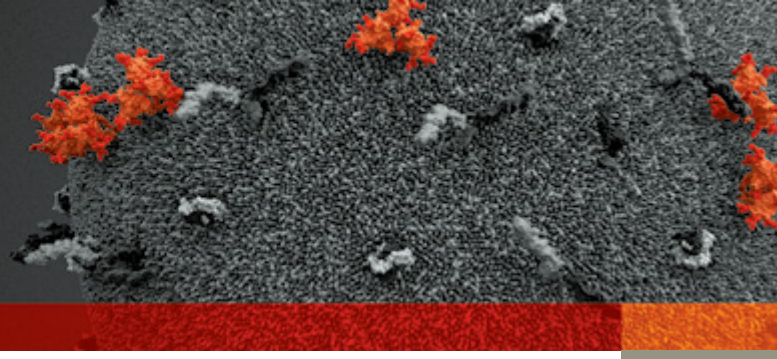
Fact Sheet



The National Institutes of Health (NIH) supports a comprehensive portfolio of clinical research on HIV infection, including both intramural and extramural clinical trials, cohort-based studies, and research consortia and collaborations. These studies are conducted in the United States and at international sites.

Clinical Trials

Clinical trials—biomedical or health-related research studies involving human volunteers—are a vital component of NIH medical research. Clinical trials conducted or supported by the NIH have resulted in landmark findings that have produced significant benefits for HIV-infected individuals and those at risk for acquiring HIV infection. For example, NIH-supported studies have demonstrated:

- The safety and efficacy of new drugs and drug combinations that can extend and improve quality of life and improve immune function in patients who are able to adhere to and tolerate antiretroviral (ARV) drugs
- The effectiveness of drug regimens on preventing and treating the many opportunistic infections, coinfections, malignancies, and clinical complications that result in HIV-related comorbidities and mortality
- Strategies to prevent mother-to-child transmission (MTCT) of HIV
- The benefits of AIDS treatment as prevention
- The critical proof of concept that an AIDS vaccine and a microbicide may be feasible and effective strategies to prevent HIV transmission.

Clinical Trials Protocols and Ethical Conduct

Clinical trials are conducted only if preliminary research shows that the intervention appears to be safe and potentially effective. Scientists develop a plan to test the intervention in human participants, known as the study protocol. The study protocol is carefully designed with input from the community (e.g., community advisory boards) and extensively reviewed by independent, external groups such as institutional review boards and ethics review committees. Extensive ethical guidelines are in place to protect patient volunteers and preserve the integrity of the science.

Information about clinical trials is available at *http://clinicaltrials.gov/ct2/info/understand*.

Clinical Trial Volunteers: Lifeblood of the Process

Clinical trial volunteers play a critical role in enhancing the scientific understanding of HIV and AIDS and in the development of new and more effective therapeutic and prevention approaches. In 2011, more than 100,000 volunteers participated in studies through NIH-funded domestic and international clinical trials networks and cohort studies. Approximately 46 percent of those participants were female.

Volunteers who participate in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and make a vital contribution to medical research.

Information about participating in NIH-supported clinical trials is available at *http://www.nih.gov/health/clinicaltrials*.

NIH HIV/AIDS Clinical Trials Networks

The NIH currently supports six HIV/AIDS clinical trials networks, managed by the National Institute of Allergy and Infectious Diseases (NIAID) with support and participation from other NIH Institutes and Centers, to conduct collaborative AIDS research. They include:

- **AIDS Clinical Trials Group (ACTG):** Supported by NIAID, the National Institute of Mental Health (NIMH), and the National Institute of Dental and Craniofacial Research (NIDCR), ACTG develops and conducts translational research and clinical trials to (1) investigate the viral and immune pathogenesis of HIV infection and its complications; (2) evaluate novel drugs and strategies for treating HIV infection; (3) evaluate interventions and strategies to treat and prevent HIV-related coinfections and comorbidity; and (4) publish and disseminate results to improve care and reduce or eliminate morbidity and mortality associated with HIV infection and its complications. *https://actgnetwork.org*
- **HIV Prevention Trials Network (HPTN):** Supported by NIAID, NIMH, the National Institute on Drug Abuse (NIDA), and the Fogarty International Center (FIC), HPTN is a worldwide collaborative clinical trials network that develops and tests the safety and efficacy of biomedical and behavioral interventions designed to prevent the acquisition and transmission of HIV. *http://www.hptn.org*
- **HIV Vaccine Trials Network (HVTN):** Supported by NIAID and NIMH, HVTN is an international collaboration to facilitate testing of preventive vaccines against HIV/AIDS that conducts all phases of clinical trials—from evaluating experimental vaccines for safety and the ability to stimulate immune responses, to testing vaccine efficacy. *http://www.hvtn.org*
- **International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT):** Supported by NIAID, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and NIMH, IMPAACT is a cooperative group of institutions, investigators, and other collaborators organized to evaluate potential therapies for HIV infection and its sequelae in infants, children, adolescents, and pregnant women. *http://impaactgroup.org*
- **International Network for Strategic Initiatives in Global HIV Trials (INSIGHT):** Supported by NIAID, NIMH, and the National Institute of Neurological Disorders and Stroke (NINDS), INSIGHT defines optimal strategies for the management of HIV and other infectious diseases through a global clinical research network. *http://insight.ccbr.umn.edu*
- **Microbicide Trials Network (MTN):** Supported by NIAID, NICHD, and NIMH, the Network brings together international investigators and community and industry partners to (1) conduct clinical trials to test topical and systemic agents; (2) develop formulations to enhance safety and product adherence; and (3) collect data to support the pharmacokinetic and pharmacodynamic correlates of safety, efficacy, and effectiveness of microbicide products for vaginal and rectal use. MTN-affiliated researchers and partners work within a unique infrastructure specifically designed to facilitate the research required to support licensure of these products for widespread use. *http://www.mtnstopshiv.org*

Network Structure

Each of these networks consists of a leadership group led by principal investigators and includes an operations center, statistical and data management center, and a laboratory. Networks have one or more clinical trials units (CTUs) and clinical research sites (CRS), located at medical schools, academic health centers, hospitals, or outpatient centers, where the clinical trials are performed. For more information about the HIV/AIDS network CTUs and CRS and a complete listing by institution, see *http://www.niaid.nih.gov/about/organization/daids/Networks/Pages/daidsnetworkunits.aspx*.

Restructuring the Clinical Trials Networks

Research institutions around the world compete for the opportunity to participate in NIH clinical trials networks. The competitive process ensures that NIH funds the most effective, productive, and innovative research organizations. The NIH's HIV/AIDS clinical trials networks undergo periodic restructuring to ensure that the best qualified research and scientifically relevant research agendas are being supported. During 2013–2014, the NIH recompeted and restructured the clinical trials networks to develop a clinical trials infrastructure best capable of performing both priority HIV/AIDS clinical research and priority research involving non-HIV/AIDS infectious diseases. The priority areas for HIV/AIDS clinical trials are HIV prevention, including HIV vaccines, microbicides, and integrated strategies to prevent HIV infection; and research toward an HIV cure and therapeutics for HIV/AIDS and associated coinfections and comorbidities in adults, adolescents, children, and pregnant women. An additional network will be dedicated to antibacterial resistance. For more information, visit *http://www.niaid.nih.gov/labsandresources/pages/default.aspx*.

Additional NIH Clinical Trials Networks

In addition to the series of networks managed by NIAID, there are several clinical trials networks supported by key NIH Institutes and Centers that address the intersection of HIV research with the priorities of their portfolio:

- **Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN):** Supported by NICHD, NIMH, and NIDA, ATN develops and conducts behavioral, community-based, translational, prophylactic, therapeutic, microbicide, and vaccine trials—both independently and in collaboration with existing research networks and individual investigators—in HIV-infected and HIV-at-risk pre-adolescents, adolescents, and young adults up to age 25. *http://www.nichd.nih.gov/research/supported*
- **AIDS Malignancy Clinical Trials Consortium (AMC):** Supported by the National Cancer Institute (NCI), this clinical trials group supports trials for treatment and management of AIDS-related cancers. *http://pub.emmes.com/study/amc/public*
- **National Drug Abuse Treatment (NDAT) Clinical Trials Network:** Supported by NIDA, the NDAT conducts studies to develop, validate, refine, and deliver new treatment options for patients in community treatment programs. *http://www.drugabuse.gov/ctn*

NIH Intramural AIDS Clinical Trials

The NIH conducts clinical trials within its intramural program on the NIH campus in Bethesda, Maryland:

- The NIH operates the world's largest clinical research hospital, the NIH Clinical Center, which conducts innovative intramural clinical research studies. A number of Institutes and Centers, including NIAID and NCI, conduct intramural AIDS protocols in the Clinical Center. *http://www.cc.nih.gov/index.html*
- NIAID also conducts early-stage HIV vaccine clinical research through its Dale and Betty Bumpers Vaccine Research Center (VRC). The VRC Clinical Trials Core Laboratory performs Phase I clinical research of HIV vaccines developed at VRC. *http://www.niaid.nih.gov/about/organization/vrc/Pages/Default.aspx*

Current NIH AIDS Clinical Research Efforts

Examples of ongoing NIH AIDS clinical trials include:

- **HPTN 052**, the study that was selected by the journal *Science* as the 2011 Breakthrough of the Year, continues to determine the long-term effectiveness and durability of two treatment strategies in preventing transmission in HIV serodiscordant heterosexual couples. *http://www.hptn.org/research_studies/hptn052.asp http://www.nih.gov/news/health/dec2011/niaid-22.htm http://www.niaid.nih.gov/news/newsreleases/2011/Pages/HPTN052.aspx*
- The **Vaginal and Oral Interventions to Control the Epidemic (VOICE)**: A Phase IIb study conducted in 5,029 women in Uganda, South Africa, and Zimbabwe that tested the safety and effectiveness of daily use of an ARV tablet (tenofovir or tenofovir/emtricitabine, also known by the brand name Truvada®) or daily use of a vaginal gel (tenofovir gel). The study found none of the products effective because most participants had not used them daily as recommended. Qualitative behavioral studies currently in progress to better understand why, despite living in communities severely affected by HIV, women did not used the products being tested. *http://www.mtnstopshiv.org/news/studies/mtn003*
- **A Study to Prevent Infection with a Ring for Extended Use (ASPIRE):** The dapivirine intravaginal ring, which is used monthly instead of daily, is currently being tested in two sister studies: the ASPIRE trial led by MTN and The Ring Study led by the nonprofit International Partnership for Microbicides (IPM). Results are expected in 2015 (MTN) and 2016 (IPM). *http://www.mtnstopshiv.org/news/studies/mtn020/factsheet*
- **Rectal Microbicides:** The first ever Phase II trial of a rectal microbicide is being tested in MTN-017. Researchers are evaluating the rectal safety, drug absorption, and acceptability of a reduced glycerin formulation of tenofovir gel, as well as oral Truvada®, among men who have sex with men (MSM) and transgender women in the United States and internationally. Results, which are are expected in early 2016, will determine whether further testing can be conducted on the effectiveness of the reduced glycerin gel in preventing the transmission of HIV from anal sex. *http://www.mtnstopshiv.org/news/studies/mtn017*

- **New Microbicide Formulations:** In the future, MTN researchers will develop and evaluate new formulations of vaginal and rectal microbicides—including new ARVs, non-ARVs, multipurpose prevention technologies to prevent HIV and either sexually transmitted infections or pregnancy—and new dosing strategies such as films, suppositories, and long-acting agents. *http://www.mtnstopshiv.org/node/706*
- The **Promoting Maternal Infant Survival Everywhere (PROMISE)** study aims to determine the optimal ARV regimen for reducing HIV MTCT during pregnancy, labor, delivery, and breastfeeding, and for preserving the health of both mother and child. *http://clinicaltrials.gov/ct2/show/NCT01061151 http://www.niaid.nih.gov/news/newsreleases/2010/Pages/PROMISE.aspx*
- The **TLC-Plus/HPTN 065** study is evaluating the feasibility of enhanced HIV testing, linkage to care, plus enhanced adherence support with treatment approach for HIV prevention in the United States. *http://clinicaltrials.gov/ct2/show/NCT01152918*
- The **Strategic Timing of Antiretroviral Therapy (START)** study is a multicenter, international, randomized trial comparing early and delayed initiation of antiretroviral therapy (ART) among relatively healthy volunteers (CD4 count >500) who have not previously received ART. A neurology substudy of the START trial also is underway to determine whether treatment initiation at higher CD4 counts provides protection against or amelioration of HIV-associated neurological disorders. *http://clinicaltrials.gov/ct2/show/NCT00867048 http://www.niaid.nih.gov/news/newsreleases/2011/Pages/START.aspx*
- The **HVTN 505 vaccine study** is a Phase II study evaluating the safety and efficacy of a multiclade HIV DNA plasmid vaccine followed by a multiclade HIV recombinant adenoviral vector vaccine in HIV-uninfected, adenovirus type 5 neutralizing antibody negative, circumcised men and male-to-female transgender persons who have sex with men. This study has been expanded to include an investigation of whether the experimental vaccine regimen prevents HIV infection, in addition to evaluating whether a two-part vaccine regimen can decrease viral load in participants who become infected. *http://www.niaid.nih.gov/news/newsreleases/2011/Pages/HVTN505expands.aspx http://www.niaid.nih.gov/news/newsreleases/2009/Pages/HVTN505.aspx*
- The **HPTN 067/ADAPT** (Alternative Dosing to Augment PrEP Pill-Taking) study is testing whether intermittent or daily PrEP dosing regimens may be more acceptable and conducive for product adherence in high-risk women and men who have sex with men. *http://www.hptn.org/research_studies/hptn067.asp*
- **AMC 075** is a study for optimization of vorinostat and combination chemotherapy with rituximab in treating patients with previously untreated HIV-related diffuse large B-cell non-Hodgkin lymphoma. *http://clinicaltrials.gov/show/NCT01193842*
- **AMC 072** is a study to determine the protective effect of the quadrivalent human papillomavirus (HPV) vaccine in HIV-infected men who have sex with men. *http://clinicaltrials.gov/show/NCT01209325*
- **AMC 071** is a multicenter trial assessing the overall survival after autologous hematopoietic stem cell transplantation and BEAM therapy of HIV-infected patients with persistent or recurrent B-cell lymphomas. *http://clinicaltrials.gov/show/NCT01141712*
- **AMC 061** is a study to determine the safety and the pharmacological interactions of administering sunitinib to HIV-infected patients with non-AIDS-defining cancers who are receiving combination ART containing protease inhibitors. *http://www.cancer.gov/clinicaltrials/search/view?cdrid=639703&version=healthprofessional*

Clinical Trials Information

For more information about AIDS clinical trials, visit *http://www.aidsinfo.nih.gov*.

For information about clinical trials in the NIH Intramural Research Program, visit *http://irp.nih.gov/nih-clinical-center/clinical-trials*.

NIAID sponsors the "Be The Generation To End the AIDS Epidemic" initiative to promote awareness, understanding, dialogue, and support for biomedical prevention research, including HIV vaccines, microbicides, and pre-exposure prophylaxis. *http://www.bethegeneration.org*

For information about clinical trials in general, visit *http://clinicaltrials.gov* or *http://www.nih.gov/health/clinicaltrials*, an NIH resource that catalogs and explains thousands of ongoing clinical studies.

Major Cohort Studies

Since the earliest days of the epidemic, the NIH has been committed to the establishment of long-term cohort studies to address the key scientific questions and challenges in populations at risk:

- The **Multicenter AIDS Cohort Study (MACS)**, sponsored by NIAID, NIDCD, and NCI, and conducted since 1984, is an ongoing prospective study of the natural and treated histories of HIV infection in homosexual and bisexual men. Data from the MACS have been the basis of more than 1,100 publications in peer-reviewed journals. *http://www.statepi.jhsph.edu/macs/macs.html*
- The **Women's Interagency HIV Study (WIHS)**, co-funded by NICHD, NIAID, NCI, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and NIDA, is the largest and longest ongoing U.S. study to investigate the impact of HIV infection on women in the United States. *http://statepiaps.jhsph.edu/wihs*
- The **Pediatric HIV/AIDS Cohort Study (PHACS)** network, sponsored by NICHD, with co-funding from NIAID, NIDA, NIDCD, NIMH, NHLBI, NIDCR, NINDS, and NIAAA, was established to address two critical pediatric HIV research questions: the long-term safety of fetal and infant exposure to prophylactic ART chemotherapy, and the effects of perinatally acquired HIV infection in adolescents. *https://phacs.nichdclinicalstudies.org/overview.asp*
- The **Veterans Aging Cohort Study (VACS)**, supported by NIAAA in collaboration with the Department of Veterans Affairs, is a prospective, observational cohort study of HIV-positive and an age/race/site-matched control group of HIV-negative veterans in care in the United States. Researchers seek to understand the role of comorbid medical and psychiatric disease in determining clinical outcomes of HIV infection. *http://www.vacohort.org*

NIH-Sponsored Research Consortia

The NIH is committed to establishing international research collaborations that address priority areas in HIV research:

- The **Center for HIV/AIDS Vaccine Immunology (CHAVI)** is a consortium of universities and academic medical centers established by NIAID to solve major problems in HIV vaccine development and design. *http://chavi.org*
- **The National NeuroAIDS Tissue Consortium (NNTC)**, supported by NINDS and NIMH, was established to collect, store, and distribute samples of nervous tissue, cerebrospinal fluid, blood, and other tissue from HIV-infected individuals. *http://www.nntc.org*
- The **Martin Delaney Collaboratory** is a funding opportunity designed to foster public–private partnerships to accelerate progress toward an HIV cure. Each research team will pursue a unique and complementary approach aimed at eradicating HIV reservoirs. *http://www.niaid.nih.gov/news/newsreleases/2011/pages/delaneycollab.aspx*
- The **International Epidemiologic Databases to Evaluate AIDS (IeDEA)** network is an international research consortium established by NIAID, with co-funding from NICHD and NCI, to collect and define key variables, harmonize data, and implement methodology to effectively pool data into large datasets to address high-priority research questions and streamline HIV/AIDS research. *http://www.iedea.org*
- The **Clinical and Translational Science Awards (CTSA)** program in the newly established National Center for Advancing Translational Sciences (NCATS) Division of Clinical Innovation supports a national consortium of medical research institutions that work together to improve the way clinical and translational research, including HIV research, is conducted nationwide to enhance its efficiency and quality. Its goals are to accelerate the process of translating laboratory discoveries into treatments for patients, to engage communities in clinical research efforts, and to train a new generation of clinical and translational researchers. *http://www.ncats.nih.gov/research/cts/ctsa/about/about.html*

- The **Centers for AIDS Research (CFAR)** program, which began in 1988 and is co-sponsored by NIAID, NCI, NICHD, the National Heart, Lung, and Blood Institute (NHLBI), NIDA, NIMH, and the National Institute on Aging (NIA), provides administrative and shared research support to synergistically enhance and coordinate high-quality AIDS research projects. CFARs accomplish this through core facilities that provide expertise, resources, and services not otherwise readily obtained through more traditional funding mechanisms. *http://www.niaid.nih.gov/labsandresources/resources/cfar/Pages/Default.aspx*

- The **CFAR Network of Integrated Clinical Systems (CNICS)** project is the first electronic medical records-based resource network poised to integrate clinical data from the large and diverse population of HIV-infected persons who are receiving care at one of the NIH-funded Centers for AIDS Research (CFAR) sites. *http://www.uab.edu/cnics*